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EXAMINER

SULLIVAN, DANIEL M

ART UNIT PAPER NUMBER

1636

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/930,593

Applicant(s)

BOONE, CHARLES

Examiner

Daniel M Sullivan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-72 is/are pending in the application.
- 4a) Of the above claim(s) 11-72 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4. 6) ☐ Other:

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 15 August 2001.

Claims 1-72 are pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-10, in Paper No. 10, filed 15 April 2003, is acknowledged.

Claims 11-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Specification

The disclosure is objected to because of the following informalities: The article "the" is missing in line 15 on page 11. Page 23, line 25 appears to contain a formatting error. Applicant is urged to review the disclosure and correct any typographical errors therein.

Appropriate correction is required.

Claim Objections

Claims 4 and 5 are objected to because of the following informalities: The claims are directed to non-elected subject matter (i.e., the input array of claim 1). Appropriate correction is required.

Double Patenting

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It is noted that copending applications 10/219,682 and 10/218,820 disclose subject matter in common with this application and may recite the same or overlapping Inventions. Since 10/219,682 and 10/218,820 are not presently available for review, no determination has been made as to whether or not a double patenting rejection over the claims from 10/219,682 or 10/218,820 should be applied to the claims of the instant application. If, upon availability of the above application to the Examiner, it is determined that there are conflicting claims between 10/219,682 or 10/218,820 and the instant application, double patenting will not be considered as new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” (See page 1117.) The specification does not “clearly allow persons of

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ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116).

The instant claims are directed to a high density output array containing at least two genetic alterations which is the mating product of two input arrays wherein at least one of the input arrays comprises multiple starting strains of yeast, wherein each starting yeast strain carries at least one genetic alteration with the genetic alteration being different in each starting yeast strain. On page 12, the specification indicates that genetic alteration encompasses: an alteration in the DNA encoding the gene; introduction of trans-dominant genetic agents; protein and RNA expression vectors of a heterologous gene from a viral, prokaryotic or eukaryotic genome, wherein the genes can be either wild type, mutated or fragmented; protein-protein interaction detection system; and a reporter whose expression reflects a change in cellular state, wherein the genetic alterations can be propagated in the yeast genome or on autonomously replicating plasmids. Thus, the claims are generic to an array of multiple yeast strains wherein the array is the mating product of any two yeast strains that are genetically modified such that the yeast comprise any alteration in any endogenous gene, any trans-dominant genetic agent, expression of any wild-type or mutant form of any heterologous gene from any and all organisms, any protein-protein interaction detection system or any reporter construct capable of indicating any and all cellular states.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). The disclosure provides detailed description of 8 species of the claimed invention consisting

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of output arrays resulting from the mating of yeast comprising mutations in the yeast *bnil*, *arc40*, *bim1*, *sgs1*, *bbc1*, *arp2*, *nbp2*, and *rad27* genes with an array of 4,644 different viable deletion strains (see especially Example 6, beginning on page 32). The Guidelines for Written Description state, “when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus” (Federal Register, Vol. 66, No. 4, Column 2, page 71436). In the instant case, the claimed genus has tremendous and widely varied scope. Clearly, the disclosure of 8 species, which differ only in the identity of a single yeast gene mutation, does not adequately reflect the variation within the genus.

As the disclosed species of the invention do not adequately describe the full scope of the claimed subject matter, it is incumbent upon Applicant to provide the relevant identifying characteristics of the invention. According to the Guidelines for written description, identifying characteristics include, “structure or other physical and/or chemical properties...functional characteristics coupled with a known or disclosed correlation between function and structure or... a combination of such identifying characteristics...” (Federal Register, Vol. 66, No. 4, page 1106, column 3, second full paragraph). In the instant case, it is important to keep in mind that the relevant identifying characteristics of the claimed output array are the phenotypic characteristics of the double mutant strains that make up the array. In the first full paragraph on page 2 of the specification, Applicant provides, “[the] arrays and the methods of analyzing such arrays of the present invention therefore fulfill a need in the art by providing simple and efficient methods for large-scale, high throughput analysis of genetic and protein-protein interactions.” As the utility of the claimed invention arises from the genetic and protein-protein interactions that can be identified therewith, a description of the claimed output arrays must include a description

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of said genetic and protein-protein interactions or at least the phenotypic characteristics of the double mutant strains of the claimed array. However, the specification is silent with regard to the phenotypic characteristics of any high-density output array other than those of the disclosed species described above.

The teachings of the specification are predominantly directed to the description of input arrays and methods of making output arrays. These teachings do not adequately describe the claimed output arrays made according to the methods because the relevant identifying characteristics of the output arrays (i.e., the phenotypes of the double mutant strains) are unpredictable. Clearly this is the case because the purpose of the claimed output arrays is to identify interactions that could not be predicted by one in possession of only the component input arrays. Thus, defining output arrays merely as the mating product of any two arrays of mutant yeast is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of all output arrays. Therefore, only the output arrays actually reduced to practice in Example 6, which provide the data set forth in Table 1, meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of “resulting yeast strain” and “resulting genetic alterations”. It is not clear from the claim exactly what the yeast strains and genetic alterations are the result of. In the interest of compact prosecution, it has been assumed that the yeast strains and genetic alterations are the result of the mating described later in the claim. However, the claim should be amended to clearly indicate how the yeast strains and genetic alterations are produced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 5 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Holzman *et al.* (1993) *J. Cell Biol.* 122:635-644 (made of record in the IDS filed 24 December 2001, Paper No. 4).

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Claim 1 is directed to a high density output array of multiple yeast strains, wherein each yeast strain in the output array comprises at least two genetic alterations, and wherein the genetic alterations are different in each yeast strain, the output array being the mating product of at least two input arrays, wherein at least one of the input arrays comprises multiple starting strains of yeast, wherein each starting yeast strain carries at least one genetic alteration, with the genetic alteration being different in each yeast strain.

Holzman *et al.* teaches an output array of multiple yeast strains comprising at least two genetic alterations, wherein the genetic alterations are different in each yeast strain, produced by mating haploid mutants of *S. cerevisiae* for the purpose of identifying complementation groups (see especially the second full paragraph in the second column on page 637, and the section entitled "Complementation Analysis" on page 636). The output array of Holzman *et al.* meets all of the limitations of the base claim, claim 1.

Further, the output array of Holzman *et al.* is diploid according to claim 2; is *S. cerevisiae* according to claims 4 and 5; is a double mutant involving mutation of two different endogenous yeast genes according to claim 7; comprises the functional deletion of two different non-essential yeast genes according to claim 8; and is a synthetic fitness double mutant according to claim 9. Thus, Holzman *et al.* teaches an output array comprising each of the limitations of the dependent claims 2, 4, 5 and 7-9.

The output array taught by Holzman *et al.* is the same as the output array claimed in the instant application; therefore, the claims are anticipated by Holzman *et al.*

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Claims 1, 2, 4-7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Uetz *et al.* (2000) *Nature* 403:623-627 (made of record in Paper No. 4).

The limitations of claim 1 are set forth herein above. Uetz *et al.* teaches an output array of multiple yeast strains comprising at least two genetic alterations (i.e., comprising a 2-hybrid bait and prey), wherein the genetic alterations are different in each yeast strain, produced by mating haploid mutants of *S. cerevisiae* for the purpose of identifying interacting proteins (see especially the section entitled "A protein array of activation-domain hybrids" beginning on page 623, and the section entitled "High-throughput screens of an activation-domain library" on page 24). The output array of Uetz *et al.* meets all of the limitations of the base claim, claim 1.

Further, the output array of Uetz *et al.* is diploid according to claim 2; is *S. cerevisiae* according to claims 4 and 5; is located on 96-well plates according to claim 6 (see especially the first full paragraph on page 624); is a double mutant comprising mutated forms (i.e., fusion constructs) of two different endogenous yeast genes according to claim 7 (i.e., the hybrid genes are endogenous to the host cell); and comprises between about 1,000 and 25 million resulting strains of yeast (i.e., 192 binding domain hybrids x about 6,000 activation domain hybrids) according to claim 10. Thus, Uetz *et al.* teaches an output array comprising each of the limitations of the dependent claims 2, 4-7 and 10.

The output array taught by Uetz *et al.* is the same as the output array claimed in the instant application; therefore, the claims are anticipated by Uetz *et al.*

Claims 1, 2, 4, 5, 7 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Ito *et al.* (2000) *Proc. Natl. Acad. Sci. USA* 97:1143-1147.

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The limitations of claim 1 are set forth herein above. Ito *et al.* teaches an output array of multiple yeast strains comprising at least two genetic alterations (i.e., comprising a 2-hybrid bait and prey), wherein the genetic alterations are different in each yeast strain, produced by mating haploid mutants of *S. cerevisiae* for the purpose of identifying interacting proteins (see especially the sections entitled “Transformation and Construction of Screening Pools” and “Screening by Mating” on page 1144). The output array of Ito *et al.* meets all of the limitations of the base claim, claim 1.

Further, the output array of Ito *et al.* is diploid according to claim 2; is *S. cerevisiae* according to claims 4 and 5; is a double mutant comprising mutated forms (i.e., fusion constructs) of two different endogenous yeast genes according to claim 7 (i.e., the hybrid genes are endogenous to the host cell); and comprises between about 1,000 and 25 million resulting strains of yeast (i.e., $\sim 4 \times 10^6$ combinations; Table 1) according to claim 10. Thus, Ito *et al.* teaches an output array comprising each of the limitations of the dependent claims 2, 4, 5, 7 and 10.

The output array taught by Ito *et al.* is the same as the output array claimed in the instant application; therefore, the claims are anticipated by Ito *et al.*

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Uetz *et al.* (2000) *Curr. Opin. Microbiol.* 3:303-308 (hereinafter Uetz *et al.* 2000a).

The limitations of claim 1 are set forth herein above. Uetz *et al.* 2000a provides a review of systematic and large-scale two-hybrid screens each of which would result in an output array of multiple yeast strains comprising at least two genetic alterations (i.e., comprising a 2-hybrid bait

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and prey), wherein the genetic alterations are different in each yeast strain, produced by mating haploid mutants of *S. cerevisiae* for the purpose of identifying interacting proteins (see especially the paragraph bridging pages 303 and 304, and the first full paragraph on 304; and Table 2). The output arrays described by Uetz *et al.* 2000a meet all of the limitations of the base claim, claim 1.

Further, the output arrays of Uetz *et al.* 2000a are diploid according to claim 2; and is *S. cerevisiae* according to claims 4 and 5. Thus, Uetz *et al.* 2000a teaches output arrays comprising each of the limitations of the dependent claims 2, 4 and 5.

The output array taught by Uetz *et al.* 2000a is the same as the output array claimed in the instant application; therefore, the claims are anticipated by Uetz *et al.* 2000a.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

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dms

June 4, 2003



**JAMES KETTER
PRIMARY EXAMINER**